European Sickle Cell Disease Cohort – Hydroxyurea – Extension study (ESCORT-HU Extension)

First published: 18/07/2024

Last updated: 03/09/2026

Study | Finalised

Administrative details

EU PAS number

EUPAS1000000066

Study ID

1000000066

DARWIN EU® study

No

Study countries

- France
- Germany
- Greece
- Italy

Study description

As safety information pertaining to the long-term use of hydroxyurea (HU) remains incomplete in spite of the first safety study (ESCORT-HU), an extension of the latter is proposed. ESCORT-HU Extension study aims at evaluating the long-term safety of Siklos® focusing on some questions regarding its safety when used in current practice in adults and paediatric patients treated with Siklos® and followed for up to 5 years.

Study status

Finalised

Research institutions and networks

Institutions

THERAVIA

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Mariane de Montalembert

Primary lead investigator

Study timelines

Date when funding contract was signed
Actual: 12/08/2020

Study start date
Actual: 12/08/2020

Data analysis start date
Planned: 06/10/2025

Actual: 02/12/2025

Date of final study report
Planned: 30/03/2026

Actual: 26/03/2026

Sources of funding

- Pharmaceutical company and other private sector

Study protocol

ESCORT-HU-EXTENSION _Protocol_V1.0 Final 20200115 signed.pdf (2.03 MB)

ESCORT-HU-EXTENSION _Protocol_V2.0 2020.10.30_clean signé.pdf (953.77 KB)

ESCORT-HU-EXTENSION__Protocol_V4.0_2023_09_19_final signed.pdf (824.98 KB)

Regulatory

Was the study required by a regulatory body?

No

Is the study required by a Risk Management Plan (RMP)?

Not applicable

Other study registration identification numbers and links

SIK-EU-20-1

NCT04707235

Methodological aspects

Study type

Study type list

Study topic:

Disease /health condition

Study type:

Non-interventional study

Scope of the study:

Drug utilisation

Evaluation of patient-reported outcomes

Safety study (incl. comparative)

Data collection methods:

Secondary use of data

Study design:

Multicentre, prospective, non-interventional cohort study

Main study objective:

The primary objective of the study is to determine the long-term safety profile of Siklos® focusing on risks which are poorly documented or unknown (unknown meaning: nature and frequency of serious adverse events causally related to Siklos® which are not listed in the product information).

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Medicinal product name

SIKLOS

Study drug International non-proprietary name (INN) or common name

HYDROXYCARBAMIDE

Anatomical Therapeutic Chemical (ATC) code

(L01XX05) hydroxycarbamide

hydroxycarbamide

Medical condition to be studied

Sickle cell disease

Additional medical condition(s)

SCD

Population studied

Short description of the study population

Male or female patients, aged ≥ 2 years old, with symptomatic sickle cell disease, treated with Siklos.

Age groups

- **Paediatric Population (< 18 years)**
  - Preterm newborn infants (0 – 27 days)
  - Term newborn infants (0 – 27 days)
  - Infants and toddlers (28 days – 23 months)
  - Children (2 to < 12 years)
  - Adolescents (12 to < 18 years)
- **Adult and elderly population (≥18 years)**
  - Adults (18 to < 65 years)
    - Adults (18 to < 46 years)
    - Adults (46 to < 65 years)
  - Elderly (≥ 65 years)
    - Adults (65 to < 75 years)
    - Adults (75 to < 85 years)
    - Adults (85 years and over)

Estimated number of subjects

2.100

Study design details

Setting

Investigators will be recruited among physicians experienced in sickle cell disease (SCD) management. Participants will be followed for up to 5 years. The study started in August 2020 and will be completed in August 2025.

Outcomes

The primary endpoint is the occurrence of malignancies, leg ulcers, male fertility impairment (oligospermia, azoospermia) and serious unexpected AEs (meaning SAEs which are not listed in the product information) according to the causal relationship with Siklos® or not and main features of these events.

Secondary endpoints are :

• Mean age at first periods for females, mean age of puberty for males and contraception,

• Incidence of the use of cryopreservation for the purpose of paternity, management of semen cryopreservation and semen analysis,

• Management of Siklos® during pregnancy and outcome of pregnancy following exposure at the time of conception or at any time during the pregnancy,

• Frequency and reason for temporary (>15 days) or permanent discontinuations of Siklos®,

• Switch or combination with alternative treatment,

• Complications linked to SCD at enrolment and occurring during follow-up,

• Quality of life for adults patients

Data analysis plan

The analyses will be mainly descriptive and no formal statistical testing will be carried out.

Summary results

A total of 2050 patients were enrolled in the study at the time of this final analysis. Among those, 2045 patients (99.8%) fulfilled the criteria for inclusion in the Safety Population. 55.6% patients of the Safety Population were females and 44.4% were males.

Median exposure duration to HU was 10 years.

During ESCORT-HU Extension study follow-up,

• 27 patients (1.3%) had a malignancy diagnosed after the start of the study.

• 128 patients (6.3%) developed leg ulcer(s) (202 events); 10 were related to HU.

• 19 patients had semen analysis. Among those, 15 patients were diagnosed with male fertility impairment: 2 qualitative abnormalities, 12 quantitative abnormalities and 3 patients with both qualitative and quantitative abnormalities.

• 4 patients experienced a SUSAR (acute spleen sequestration, hypogonadism, retinal micro bleeding, type 2 diabetes).

• 138 pregnancies were reported in 111 female patients: 69 pregnancies were with normal birth (50.7%) and 17 with premature birth (12.5%). Forty-two (42) pregnancies (30.9%) were reported without living child, 6 were ongoing, data was missing for 2 pregnancies and 2 had unknown outcome. Among those, Siklos® treatment had not been interrupted before conception in 28 cases.

• 34 pregnancies were reported in 30 male patients: 27 with normal birth (88.2%), 3 (8.8%) without living child, and 1 (2.9%) pregnancy was ongoing. Among those, Siklos® treatment had not been interrupted before conception in 17 cases.

Documents

Study report

ESCORT-HU2_PASS_Final_Report_V1.0_20260326 (3).pdf (10.5 MB)

ESCORT-HU2_PASS_Interim_Report_4_V1.0_20240905 signed.pdf (1.62 MB)

Data management

ENCePP Seal

The use of the ENCePP Seal has been discontinued since February 2025. The ENCePP Seal fields are retained in the display mode for transparency but are no longer maintained.

Data sources

Data sources (types)

Non-interventional study

Use of a Common Data Model (CDM)

CDM mapping

Yes

Data quality specifications

Check conformance

Yes

Check completeness

Yes

Check stability

Yes

Check logical consistency

Yes

Data characterisation

Data characterisation conducted

Yes

Data characterisation details

Data QC is performed in all sites in each country involved in the study. In each site, following an iterative approach, 5% of the participants undergo QC. Each CRF page is reviewed completely (100%) by the Clinical Research Associate for accuracy and completion. If the control is not satisfying (% of error >5%), other 5% of participants undergo QC. Furthermore, regular remote monitoring is performed in order to check missing data, inconsistent data and compliance to the study protocol.